

Claims

What is claimed is:

1. A compound wherein a residue of a compound of formula I (Figure 1) is linked to one or more peptide residues or amino acid residues wherein: 1) at least one of the peptide residues or the amino acid residues is linked to one or more chelating groups comprising one or more metallic radionuclides; or 2) at least one of the peptide residues or the amino acid residues comprises one or more non-metallic radionuclides; or a pharmaceutically acceptable salt thereof.
2. The compound of claim 1 wherein at least one of the one or more metallic radionuclides is a diagnostic radionuclide.
3. The compound of claim 1 wherein at least one of the one or more metallic radionuclides is a therapeutic radionuclide.
4. The compound of claim 1 wherein at least one of the one or more non-metallic radionuclides is a diagnostic radionuclide.
5. The compound of claim 1 wherein the residue of a compound of formula I is linked to a peptide residue or an amino acid residue at the position of the b-carboxamide, d-carboxamide, e-carboxamide, or the 6-position of the compound of formula I.
6. The compound of claim 1 wherein the residue of a compound of formula I is linked to a peptide residue or an amino acid residue at the position of the b-carboxamide of the compound of formula I.
7. The compound of claim 1 wherein the residue of a compound of formula I is linked to a peptide residue or an amino acid residue at the d-carboxamide of the compound of formula I.

8. The compound of claim 1 wherein the residue of a compound of formula I is linked to a peptide residue or an amino acid residue at the ϵ -carboxamide of the compound of formula I.
9. The compound of claim 1 wherein the residue of a compound of formula I is linked to a peptide residue or an amino acid residue at the 6-position of the compound of formula I.
10. The compound of claim 1 wherein at least one peptide residue comprises 2 to about 20 amino acids.
11. The compound of claim 10 wherein at least one peptide residue is a residue of poly-L-lysine.
12. The compound of claim 1 wherein at least one peptide residue is linked to more than one chelating group.
13. The compound of claim 1 wherein at least one peptide residue is linked to 2 to about 4 chelating groups.
14. The compound of claim 1 wherein at least one chelating group is EDTA, DTPA, TETA, DOTA, DOTMP, DCTA, or MAG3.
15. The compound of claim 1 wherein at least one chelating group is DTPA.
16. The compound of claim 1 wherein each metallic radioisotope is independently Antimony-124, Antimony-125, Arsenic-74, Barium-103, Barium-140, Beryllium-7, Bismuth-206, Bismuth-207, Cadmium-109, Cadmium-115m, Calcium-45, Cerium-139, Cerium-141, Cerium-144, Cesium-137, Chromium-51, Cobalt-56, Cobalt-57, Cobalt-58, Cobalt-60, Cobalt-64, Copper-67, Erbium-169, Europium-152, Gallium-64, Gadolinium-153, Gadolinium-157, Gold-195, Gold-199, Hafnium-175, Hafnium-175-181, Holmium-166, Indium-111,

Iridium-192, Iron-55, Iron-59, Krypton-85, Lead-210, Manganese-54, Mercury-197, Mercury-203, Molybdenum-99, Neodymium-147, Neptunium-237, Nickel-63, Niobium-95, Osmium-185 + 191, Palladium-103, Platinum-195m, Praseodymium-143, Promethium-147, Protactinium-233, Radium-226, Rhenium-186, Rhenium-188, Rubidium-86, Ruthenium-103, Ruthenium-106, Scandium-44, Scandium-46, Selenium-75, Silver-110m, Silver-111, Sodium-22, Strontium-85, Strontium-89, Strontium-90, Sulfur-35, Tantalum-182, Technetium-99m, Tellurium-125, Tellurium-132, Thallium-204, Thorium-228, Thorium-232, Thallium-170, Tin-113, Tin-114, Tin-117m, Titanium-44, Tungsten-185, Vanadium-48, Vanadium-49, Ytterbium-169, Yttrium-86, Yttrium-88, Yttrium-90, Yttrium-91, Zinc-65, or Zirconium-95.

17. The compound of claim 1 wherein a residue of a compound of formula I is linked to a residue of formula $-\text{NHCH}[(\text{CH}_2)_4\text{NH}_2\text{-DET}]\text{CO-}]_n\text{-Q}$ wherein Q is H, $(\text{C}_1\text{-C}_{14})$ alkyl, or a suitable carboxy protecting group; and DET is a chelating group residue comprising a metallic radionuclide and wherein n is between 2 and about 20.

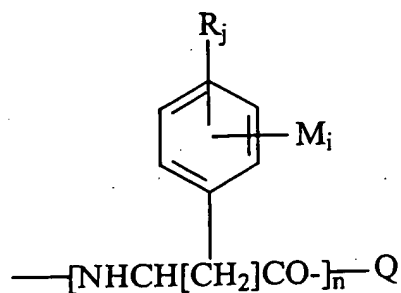
18. The compound of claim 17 wherein the chelating group is DTPA.

19. The compound of claim 1 wherein the residue of a compound of formula I is linked to two peptide residues, two amino acid residues, or an amino acid residue and a peptide residue wherein at least one peptide residue or at least one amino acid residue is linked to one or more chelating groups comprising one or more metallic radionuclides.

20. The compound of claim 1 wherein at least one peptide residue comprises more than one non-metallic radionuclide.

21. The compound of claim 1 wherein at least one amino acid residue comprises more than one non-metallic radionuclide.

22. The compound of claim 1 wherein at least one peptide residue comprises 2 to about 4 non-metallic radionuclides.
23. The compound of claim 1 wherein at least one amino acid residue comprises 2 to about 4 non-metallic radionuclides.
24. The compound of claim 1 wherein each non-metallic radionuclide is independently Fluorine-18, Bromine-76, or Iodine-123.
25. The compound of claim 1 wherein the residue of a compound of formula I is linked to two peptide residues, two amino acid residues, or a peptide residue and an amino acid residue wherein at least one of the peptide residues or at least one of the amino acid residues comprises one or more non-metallic radionuclides.
26. The compound of claim 1 wherein at least one peptide residue has the formula

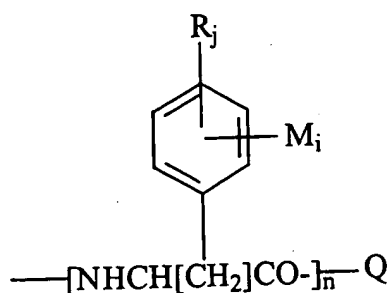


wherein each M is independently a non-metallic radionuclide; each R is independently (C_1-C_{14}) alkyl, (C_2-C_{14}) alkenyl, (C_2-C_{14}) alkynyl, (C_1-C_{14}) alkoxy, hydroxy, cyano, nitro, halo, trifluoromethyl, $N(R_a)(R_b)$, (C_1-C_{14}) alkanoyl, (C_2-C_{14}) alkanoyloxy, (C_6-C_{10}) aryl, or (C_3-C_8) cycloalkyl wherein R_a and R_b are each independently H or (C_1-C_{14}) alkyl; Q is H , (C_1-C_{14}) alkyl, or a suitable amino protecting group; n is 2 to about 20; and wherein i is 1-5, j is 0-4 and $i+j \leq 5$.

27. The compound of claim 26 wherein each M is independently Fluorine-18, Bromine-76, or Iodine-123.
28. A compound wherein a residue of a compound of formula I is linked to one or more residues of the formula $-\text{NHCH}[(\text{CH}_2)_4\text{NH}_2\text{-DET}]\text{CO}-]_n$ - Q wherein Q is H, $(\text{C}_1\text{-C}_{14})$ alkyl, or a suitable carboxy protecting group; and DET is a chelating group residue comprising a metallic radionuclide and wherein n is between 2 and about 20; or a pharmaceutically acceptable salt thereof.
29. The compound of claim 28 wherein the chelating group is DTPA.
30. The compound of claim 28 wherein each metallic radionuclide is independently Antimony-124, Antimony-125, Arsenic-74, Barium-103, Barium-140, Beryllium-7, Bismuth-206, Bismuth-207, Cadmium-109, Cadmium-115m, Calcium-45, Cerium-139, Cerium-141, Cerium-144, Cesium-137, Chromium-51, Cobalt-56, Cobalt-57, Cobalt-58, Cobalt-60, Cobalt-64, Copper-67, Erbium-169, Europium-152, Gallium-64, Gadolinium-153, Gadolinium-157, Gold-195, Gold-199, Hafnium-175, Hafnium-175-181, Holmium-166, Indium-111, Iridium-192, Iron-55, Iron-59, Krypton-85, Lead-210, Manganese-54, Mercury-197, Mercury-203, Molybdenum-99, Neodymium-147, Neptunium-237, Nickel-63, Niobium-95, Osmium-185 + 191, Palladium-103, Platinum-195m, Praseodymium-143, Promethium-147, Protactinium-233, Radium-226, Rhenium-186, Rhenium-188, Rubidium-86, Ruthenium-103, Ruthenium-106, Scandium-44, Scandium-46, Selenium-75, Silver-110m, Silver-111, Sodium-22, Strontium-85, Strontium-89, Strontium-90, Sulfur-35, Tantalum-182, Technetium-99m, Tellurium-125, Tellurium-132, Thallium-204, Thorium-228, Thorium-232, Thallium-170, Tin-113, Tin-114, Tin-117m, Titanium-44, Tungsten-185, Vanadium-48, Vanadium-49, Ytterbium-169, Yttrium-86, Yttrium-88, Yttrium-90, Yttrium-91, Zinc-65, or Zirconium-95.
31. The compound of claim 28 wherein n is about 8 to about 11.

32. The compound of claim 28 wherein the residue of a compound of formula I is linked to two residues of the formula $P-[NHCH[(CH_2)_4NH_2-DET]CO-]_n-Q$ wherein P is H, (C₁-C₁₄)alkyl, or a suitable amino protecting group; Q is H, (C₁-C₁₄)alkyl, or a suitable carboxy protecting group; and DET is independently a chelating group residue comprising a metallic radionuclide and wherein n is 2 to about 20.

33. A compound wherein a residue of a compound of formula I is linked to one or more residues of the formula



wherein each M is independently a non-metallic radionuclide; wherein each R is independently (C₁-C₁₄)alkyl, (C₂-C₁₄)alkenyl, (C₂-C₁₄)alkynyl, (C₁-C₁₄)alkoxy, hydroxy, cyano, nitro, halo, trifluoromethyl, N(R_a)(R_b), (C₁-C₁₄)alkanoyl, (C₂-C₁₄)alkanoyloxy, (C₆-C₁₀)aryl, or (C₃-C₈)cycloalkyl wherein R_a and R_b are each independently H or (C₁-C₁₄)alkyl; Q is H, (C₁-C₁₄)alkyl, or a suitable amino protecting group; n is 2 to about 20; and wherein i is 1-5, j is 0-4 and i+j is ≤ 5; or a pharmaceutically acceptable salt thereof.

34. The compound of claim 33 wherein each M is Fluorine-18, Bromine-76, or Iodine-123.

35. The compound of claim 33 wherein i is 1.

36. The compound of claim 33 wherein j is 0.

37. The compound of claim 1 wherein the residue of a compound of formula I is further linked to one or more detectable radionuclides.
38. The compound of claim 37 wherein the detectable radionuclide is a non-metallic radionuclide.
39. The compound of claim 38 wherein the non-metallic radionuclide is Carbon-11, Fluorine-18, Bromine-76, Iodine-123, or Iodine-124.
40. The compound of claim 37 wherein the detectable radionuclide is directly linked to the compound of formula I.
41. The compound of claim 37 wherein the detectable radionuclide is linked by a linker to the compound of formula I.
42. The compound of claim 41 wherein the linker is of the formula W-A wherein A is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₃-C₈)cycloalkyl, or (C₆-C₁₀)aryl, wherein W is -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -N(R)-, -C(=O)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl; and wherein A is linked to one or more non-metallic radionuclides.
43. The compound of claim 41 wherein the linker is about 5 angstroms to about 50 angstroms, inclusive, in length.
44. The compound of claim 41 wherein the linker is linked to the 6-position of the compound of formula I or is linked to the residue of a-, b-, d- or e-carboxamide group of the compound of formula I.
45. A compound wherein a residue of a compound of formula I is linked to a residue of a peptide which is linked to one or more chelating groups comprising a metallic radionuclide; or a pharmaceutically acceptable salt thereof.

46. A compound wherein a residue of a compound of formula I is linked to a residue of an amino acid which is linked to one or more chelating groups comprising a metallic radionuclide; or a pharmaceutically acceptable salt thereof.
47. A compound wherein a residue of a compound of formula I is linked to a residue of a peptide comprising one or more non-metallic radionuclides; or a pharmaceutically acceptable salt thereof.
48. A compound wherein a residue of a compound of formula I is linked to a residue of an amino acid comprising one or more non-metallic radionuclides; or a pharmaceutically acceptable salt thereof.
49. A compound wherein a residue of a compound of formula I (Figure 1) is linked to one or more non-metallic radionuclides; or a pharmaceutically acceptable salt thereof.
50. The compound of claim 49 wherein the non-metallic radionuclide is Carbon-11, Fluorine-18, Bromine-76, Iodine-123, or Iodine-124.
51. The compound of claim 49 wherein the detectable radionuclide is directly linked to the compound of formula I.
52. The compound of claim 49 wherein the detectable radionuclide is linked by a linker to the compound of formula I.
53. The compound of claim 52 wherein the linker is of the formula W-A wherein A is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₃-C₈)cycloalkyl, or (C₆-C₁₀)aryl, wherein W is -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O)-, -S(O)₂-, -N(R)-, -C(=O)-, or a direct bond; wherein each R is independently H or (C₁-C₆)alkyl; and wherein A is linked to one or more non-metallic radionuclides.

54. The compound of claim 52 wherein the linker is about 5 angstroms to about 50 angstroms, inclusive, in length.
55. The compound of claim 52 wherein the linker is linked to the 6-position of the compound of formula I or is linked to the residue of a-, b-, d- or e-carboxamide group of the compound of formula I.
56. A pharmaceutical composition comprising a compound of any one of claims 1-55 and a pharmaceutically acceptable carrier.
57. A method for imaging a tumor in mammalian tissue comprising administering to the mammal an amount of a compound of any one of claims 1-55; and detecting said compound.
58. The method of claim 57 wherein the mammal is a human.
59. The method of claim 57 wherein the mammalian tissue is located in the breast, lung, thyroid, lymph node, genitourinary system, musculoskeletal system, gastrointestinal tract, central or peripheral nervous system, head, neck, or heart.
60. A method for treating a tumor in a mammal comprising administering to the mammal an effective therapeutic amount of a compound of any one of claims 1-55; wherein said compound comprises at least one therapeutic radionuclide.
61. The method of claim 60 wherein the mammal is a human.
62. The method of claim 60 wherein the mammalian tissue is located in the breast, lung, thyroid, lymph node, genitourinary system, musculoskeletal system, gastrointestinal tract, central or peripheral nervous system, head, neck, or heart.

63. A compound of any one of claims 1-55 for use in medical therapy or diagnosis.

64. The use of a compound of any one of claims 1-55 for the manufacture of a medicament for imaging a tumor in a mammal.

65. The use of a compound of claim 64 wherein the mammal is a human.

66. The use of a compound of claim 64 wherein the mammalian tissue is located in the breast, lung, thyroid, lymph node, genitourinary system, musculoskeletal system, gastrointestinal tract, central or peripheral nervous system, head, neck, or heart.

67. The use of a compound of any one of claims 1-55 for the manufacture of a medicament for treating a tumor in a mammal.

68. The use of a compound of claim 67 wherein the mammal is a human.

69. The use of a compound of claim 67 wherein the mammalian tissue is located in the breast, lung, thyroid, lymph node, genitourinary system, musculoskeletal system, gastrointestinal tract, central or peripheral nervous system, head, neck, or heart.